Measurement of HEPA filter performance using the dispersed oil particle (DOP) aerosol test for leak detection in filter installations

Edition 3

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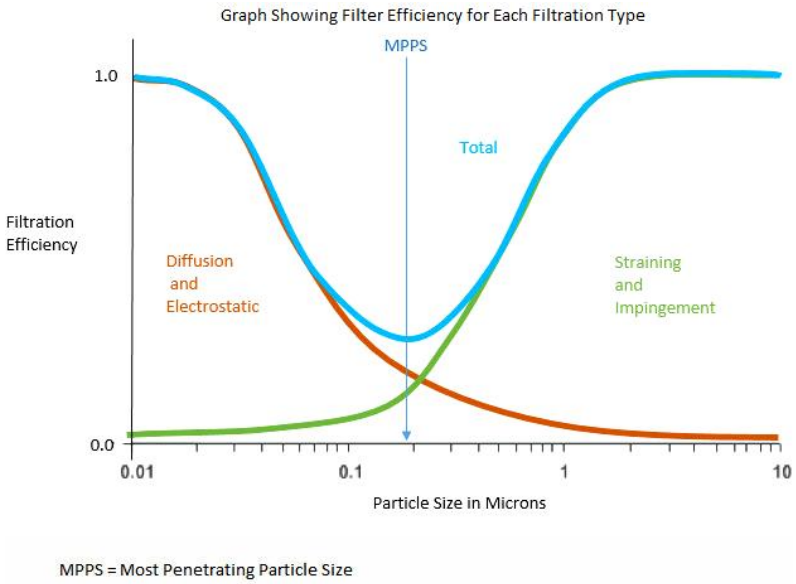
Document History	Issue date and reason for change
Edition 1	Issued April 2006 Developed by the members of the Microbiology Protocols Group (T Munton; P Hunt; J Rhodes)
Edition 2	Issued April 2008 Amended to update standards and tables and to include updated PD 6609, 2007
Edition 3	Issued Dec 2018 Amended to update standards and table and to include updated BS EN 1822 2009 and additional clarification. Guidance for purchase and fitting replacement filters has been added.
Edition 4	

This test protocol is supplementary to Quality Assurance of Aseptic Preparation Services, Fifth edition, Edited by Alison M Beaney, Pharmaceutical Press, 2016.

1. Introduction

The purpose of HEPA filters in cleanrooms, controlled environments, workstations and cabinets is to control particles and microbes so that environmental standards can be maintained and the particulate and microbiological challenge to processing is minimised. HEPA filters may also be used to provide operator protection in safety cabinets.



For NHS Pharmaceutical Aseptic preparation there is a reliance on a clean air device to provide an environment that meets EU GMP microbial standard of <1cfu/m^3 air. To ensure compliance the filter and housing should not allow a viable particle to enter the work area. A grade B cleanroom 'in use' should have microbial bioburden of ≤10cfu/m^3 air. To ensure that the limit is not exceeded 'in use'; the 'at rest' bioburden should be kept to a minimum.

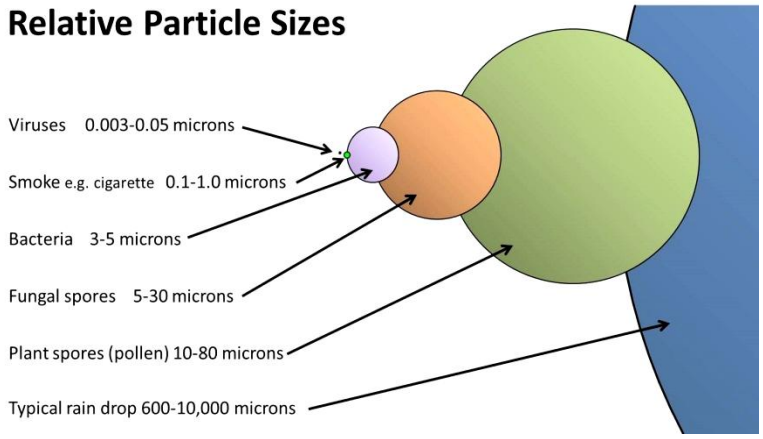
This document has been developed to provide guidance to the testing of NHS aseptic preparation facilities.

Small particles are retained by either diffusion (Brownian motion causes the particle to move in an irregular pattern increasing its chance of making contact with and adhering to the fibres in the filter) or by electrostatic charges (The particulate is attracted to the media though an electrostatic charge. This is generally only in synthetic media and very often this electrostatic charge diminishes with time and/or humidity). Larger particles are trapped by filter media by either straining (the physical capture of a particle by the fibres or holes in a media preventing it passing due to their relative size) or impingement (the particle physically hits and sticks to the fibre).

The DOP test is used to detect leaks in HEPA (high efficiency particulate air) filters in their operational conditions. It applies to all clean rooms and clean air devices. The test is intended to test the filter, seals, housing and terminal ductwork and, in addition to testing filter integrity, ensures that all air entering the controlled environment passes through the HEPA filtration system. The test should be applied to all new HEPA filters and the results assessed before cleaning and bringing the room or device back into use. It also used as part of a requalification programme as set out in a validation master plan. The most penetrating particle size (MPPS) is the particle size that is most likely to pass through a filter. For HEPA

filters it is usually between 0.2µ and 0.3µ. It is the particle size used to rate the filter using BS EN 1822-1:2009 classification (see appendix 1).

The test method used is that described in BS EN 14644-3:2005 *"Cleanrooms and associated controlled environments – Part 3: Test methods"* and in PD6609:2007 "*Environmental cleanliness in enclosed spaces – Guide to in situ high efficiency filter leak testing"*, an explanatory supplement to BS EN 14644-3:2005. In this test an aerosol is dispersed upstream of the filter and the downstream face and seals of the filter are scanned for leaks.



Fungal spores are relatively large and easy to retain, whereas individual bacteria are smaller in size and a proportion could pass through a filter.

For this reason; the following is recommended for use in NHS clean rooms:

- **EU GMP Grades A & B** – **H14** with overall efficiency of 99.995% at MPPS
- **EU GMP Grades C & D** – **H13** with overall efficiency of 99.95% at MPPS

Analysts involved in this area of testing must be trained in and familiar with the following:

- The requirements of BS EN ISO 14644-3 (B.6)
- The requirements of PD6609:2007
- Correct use of the photometer and aerosol generator used
- Current GMP requirements
- Good clean-room practice

They should hold a recognised qualification in DOP testing e.g. Cleanroom Testing and Certification Board (CTCB) professional certification or equivalent.

The DOP test is an in situ test of a filter using a range of particle sizes and not just the MPPS particle size. For this reason the results for the BS EN 1822-1:2009 and PD6609:2007 are **not** comparable.

NOTE: Upon publication of BS EN ISO 14644-3, PD 6609:2000 and all parts of BS 5295:1989 were withdrawn. PD 6609:2007 is supplementary to BS EN ISO 14644-3.

2. Replacement Filters

New filters should be ordered with reference to this guidance (see appendix 2) and fitted by competent personnel wearing garments appropriate to the room classification.

When purchasing replacement filters for grade B rooms the ability of the air handling system to cope with the pressure resistance should be assessed to ensure the design airflow can be provided. This can be achieved by reference to the cleanroom design and Operational Qualification.

The supplier of an H14 filter should be informed on the purchase order that the filter will be tested to a DOP penetration of 0.001%.

Filters are often heavy and difficult to manoeuvre into place without causing damage and therefore a method statement and risk assessment should be sought. New filters usually have a certificate of analysis providing the filter details and BS EN 1822 test results. This should be retained and the housing details recorded to indicate where the filters were installed. It is advisable to have filter removal and fitting witnessed by quality assurance personnel or person acting on their behalf.

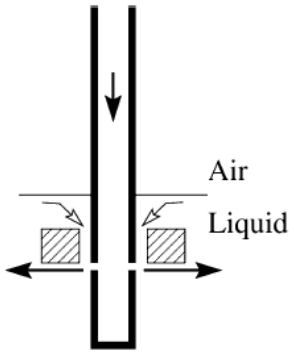
3. DOP Test Equipment

3.1 **An aerosol generator** capable of generating a polydisperse aerosol of the test oil.

BS EN ISO 14644-3 specifies a number of test oils. Shell Ondina EL is the test oil normally used in the UK. Shell Ondina Oils, sometimes referred to as medicinal white oils, are highly refined, paraffinic white mineral oils, additive-free and aromatic-free. See appendix 5 for details of the hazard data sheet for Ondina X 420.

Other test oils are used in the USA, e.g. Durasyn® 164 polyalphaolefin which is a hydrogenated synthetic hydrocarbon base fluid with a viscosity of 4 centistokes. Contractors operating in both the UK and the USA may choose to use this oil or similar.

The distribution of particles in the aerosol is described in BS EN ISO 14644-3 (B.6.6.2) and further explained in PD 6609:2007 at 3.2 which states “BS EN ISO 14644-3:2005 considers that the mass median particle size of the test aerosol should be between 0.5µm and 0.7 µm with a geometric standard deviation of up to 1.7. This is a size distribution typical of that produced by a Laskin nozzle.



Laskin Nozzle Process:

Compressed air is forced through a nozzle submerged in a liquid to create a high concentration of small liquid droplets in a polydisperse aerosol.

As the compressed air flows at high velocity out of the radial holes, oil is drawn in to the airflow and effectively atomised into the small air bubbles created, which then grow and move to the surface of the liquid where they burst, releasing the generated particles they contain into the air above the liquid.

The original principle and design dates back to 1948

However, it is known that the mass median particle diameter of particles produced by a **thermal generator** is likely to be below the size suggested by BS EN ISO 14644-3:2005 and closer to the most penetrating particle size (MPPS) of high efficiency filters. It is therefore likely that more leaks will be found when a thermal generator is used, but this is not considered a disadvantage.

The **upstream aerosol challenge** should be between **20 mg/m^3 (µg/l)** and **80 mg/m^3 (µg/l).** It should be homogeneous and remain uniform from the start to the finish of each individual test.

The generator must have sufficient output to ensure that an adequate upstream concentration can be achieved in the installation under test.

The aerosol generator should be serviced and tested annually, using an aerosol photometer that has been calibrated for the oil being used in the generator, and a certificate obtained to certify that it is performing in accordance with the manufacturer's specification. Full calibration is unnecessary and very expensive.

3.2 A photometer capable of estimation of mass concentration of airborne particles of the aerosol described in 2.1 with an accuracy of better than +5% over a range of 0.001% to 100% of the test aerosol.

The photometer should have a minimum threshold sensitivity of 0.00002 mg/m3 (µg/l)* [so as to register a penetration of 0.001% against the minimum upstream challenge of 20 mg/m3 (µg/l)] and be capable of measuring the maximum aerosol challenge concentration of 80 mg/m3 (µg/l) of aerosol.

A linear photometer is preferable to a logarithmic photometer because it is capable of indicating % penetration directly and is more likely to meet the threshold sensitivity requirement. Logarithmic photometers should not be used to test for penetrations less than 0.01%, as they do not meet the required threshold sensitivity. They are no longer manufactured but some old equipment may be in use.

The photometer should be serviced and calibrated annually with an aerosol of the test oil that is normally used, and a calibration certificate obtained.

***** This threshold sensitivity is lower (more sensitive) than in BS EN ISO 14644-3 so that the photometer can detect penetrations down to 0.001%. (BS EN ISO 14644-3 states "Designated leaks are deemed to have occurred where a reading greater than 0.01% of the upstream challenge aerosol concentration. Alternative acceptance criteria may be agreed between the customer and the supplier"). Modern spectrophotometers have a 0.001% setting.

4. Pre- test conditions

The test is performed with the installation in its operational condition at its designed airflow rate, in a balanced condition with any pre-filters removed. The refrigeration, heating and humidification circuits of the plant (if fitted) must be turned off prior to testing to avoid attenuation of the aerosol challenge. Diffusers must be removed from filters before scanning to enable adequate access to the filter face, housing and seals.

> **Note:** Pre-filters may be left in place and refrigeration, heating and humidification circuits left on if the aerosol is introduced into the duct downstream of these components. If testing is performed in this way, the aerosol is likely to be introduced after the fan, necessitating the use of an aerosol injection pump to overcome the pressure in the system. The length of ductwork between the introduction of the aerosol and the filters will be reduced and this may adversely affect mixing of the aerosol with the air stream.

Indoor plant and/or suite smoke detectors should be disabled for the duration of the test and a period to allow any DOP to be removed (usually 20 minutes for a suite, but may be longer for an indoor air handling unit). This usually has to be arranged in advance and it is important to check that it has been actioned before starting a test.

It is advisable to have the test witnessed by trained quality assurance personnel or person acting on their behalf. Guidance is given in appendix 4.

5. Aerosol injection

The aerosol is injected upstream of the filter sufficiently far upstream to ensure adequate mixing of the aerosol and air stream and ensure even distribution over the filter face. This is typically 15-20 duct diameters upstream.

An aerosol injection pump may be required to inject aerosol into pressurised parts of the system. The ports used for introducing and measuring the aerosol concentration must be capable of being effectively sealed when not in use.

Where the required mixing distance of 15 – 20 duct diameters cannot be achieved, the aerosol should be introduced using a distribution system such as sparge pipes. This is known as distributing the aerosol at the point of injection.

Access Points:

Suitable ports should be fitted to the air handling plant to enable introduction of an adequate level of aerosol challenge upstream of the filters. Each filter terminal should also be fitted with a re-sealable sample port to enable the upstream aerosol concentration to be measured.

In cases where an upstream sample point has not been included in the design of the equipment or where the equipment has been installed in such a way that the sample point is not accessible, then an appropriate sample point must be fitted before testing can start.

6. Upstream measurement of aerosol concentration

The upstream concentration of aerosol must be adjusted until it is in the range 20 – 80 mg/m3 (µg/l).

Measurement should be as close as possible to, and preferably no more than 50mm upstream of, the filter. If more than one filter is served by the ductwork, distribution in branches of the ducting may not be uniform. For this reason it is essential that upstream concentration is measured at each filter.

The concentration should be checked over a short period of time to establish that it is a stable concentration. Care should be taken not to measure high concentrations of aerosol over long periods of time as this may saturate the optical cell in the photometer. When a stable reading in the specified range has been achieved, the concentration should be recorded. The upstream concentration can be used subsequently to calculate percentage penetration when the downstream measurement has been made. Alternatively the linear photometer may be operated in the percentage penetration mode using the upstream concentration as a 100% reference reading. The downstream reading is then shown as the percentage penetration.

The upstream concentration should be checked and recorded at the end of each test to confirm that it is the same as at the start (usually within 10%).

7. Downstream measurements of aerosol concentration

Scanning is performed with a suitable fishtail probe attached to the photometer inlet tubing. After setting the photometer as described in 6., the filter face should be scanned in overlapping scans approximately 30mm from the filter face at a rate derived from the formula in BS EN ISO 14644-3:2005 (B.6.2.5), which says that the scan rate should be approximately 15/Wp cm/s, where Wp is the probe dimension perpendicular to the scan direction. If the probe is 3 cm wide, the scan rate is 5 cm/s.

The filter seal and any exposed parts of the housing and ductwork should also be scanned. In order to facilitate proper scanning, any diffusers fitted must be removed to enable access.

When testing for leaks between a HEPA filter and its housing, the leak may be into a recess or ‘dead zone’ where there is no natural airflow. The concentration of the challenge aerosol is likely to build up in this ‘dead zone’. Therefore, when a high reading is indicated in such a situation, the photometer probe should be held in the same spot until the accumulated challenge aerosol has been cleared by the air drawn into the probe (which is typically at a rate of 28 litres/min) and a steady reading obtained. This steady reading is the one that should be used to determine whether the leak is within the specified limits. Alternatively the ‘dead zone’ may be flushed with source of HEPA-filtered air to clear the accumulated aerosol until a steady reading is obtained.

8. Leak integrity of facility

The aerosol generator and photometer may also be used to check for leaks into the controlled environment from surrounding non-controlled areas at the same or different static pressures. These leaks may be through construction joints, service conduits, light fittings and other fittings, and may be caused by induction or by pressurisation of ceiling and other voids. A suitable test is described in BS EN ISO 14644-3:2005: B.13 - Containment leak test.

This test should be carried out on **all** HEPA filter housings to ensure that unfiltered air does not enter around the filter. The test should be carried out on the ductwork if there is no terminal HEPA filter into a clean room. Smoke should be generated around the supply ductwork and the air scanned as it enters the cleanroom. It is recommended that the facility is inspected annually for potential leaks and the leak test is carried out where appropriate.

9. Limits

The **limits** to be used for aerosol penetration in NHS filter installations and facilities are:

- EU GMP Grades A & B environments – maximum penetration = 0.001%
- EU GMP Grades C & D environments – maximum penetration = 0.01%

HEPA filters are tested by the manufacturer as described in BS EN 1822:2010 standards. H14 filters are expected to be ten times more efficient than H13 filters. Good quality H14 filters have been shown to provide similar results when DOP tested in situ.

The BS EN BS EN 1822-1:2009 filter class descriptions are:

- **EPA 10 - EPA 12: Efficiency Particulate Air Filters**
- **HEPA 13 - HEPA 14: High Efficiency Particulate Air Filters**
- **ULPA 15 - ULPA 17: Ultra Low Penetration Air Filters**

Leak integrity of facility – BS EN ISO 14644-3:2005: B.13 gives the limit for leaks into the controlled environment as 0.01% maximum penetration. It may however, be difficult to measure the concentration of the upstream challenge in this test, in which case it becomes a leak detection test.

A leak shall be deemed to have occurred if a steady repeatable reading on the photometer at any point exceeds the maximum penetration value. Temporary repairs are permitted in certain circumstances – see appendix 3.

10. Reporting of results

A test report is prepared and contains at least the following information: -

- Name and address of the organisation performing the test.
- Analyst name and qualifications.
- Unique test reference number.
- Name and location of client and contact person and/or witness person.
- Filter or cabinet ID and location.
- Date of the test and date report completed.
- The upstream aerosol concentration at the beginning and end of the test for each filter.
- The maximum downstream concentration detected for each filter.
- Result of testing including a statement to indicate pass or fail for each filter.
- Any action taken and/or recommendations.
- Signature of person approving the report.
- Photometer calibration details.
- Generator service details.

APPENDICES

APPENDIX 1: Grades of filters used in controlled environments

Filter manufacturers use BS EN 1822:2010 series of standards to classify filters by their Overall Efficiency against the MPPS (most penetrating particle size). The MPPS is normally between 0.1 and 0.3µm.

The following table shows the BS EN 1822-1:2009 classification: -

Grade	Overall % Efficiency @ MPPS	Local % Penetration @ MPPS
E10	85	-
E11	95	-
E12	99.5	-
H13	99.95	0.25
H14	99.995	0.025
U15	99.9995	0.0025
U16	99.99995	0.00025
U17	99.999995	0.0001

There are major differences between the manufacturers test (BS EN 1822) and the in situ DOP test (PD 6609) which does not allow a direct comparison between the results. The BS EN 1822 test uses a narrow range of particle size at the maximum penetration particle size (MPPS) whereas DOP particle size is much broader and only a small percentage of the challenge will be at MPPS.

The BS EN 1822 test is an average result over the whole surface of the filter and not a point test result as described in PD 6609. Therefore filters with up to 0.25% MPPS penetration can be classified as H13 provided the average result is less than 0.05% penetration. Note these filters are expected to pass a DOP test of 0.01%.

The BS EN 1822 test is carried out at a set air velocity, often 0.45m/s and the value is recorded on the certificate. The DOP test is carried out at the actual supply velocity provided by the air handling unit.

APPENDIX 2: Filter purchase

Filters should be supplied with a suitable casing to support the filter medium. This casing is preferably metal. Casings made of wooden materials such as MDF or chipboard are not recommended.

The type of filter sealing mechanism should be specified based on the housing design. There are gel filled seals, rounded gaskets and flat gaskets. Gaskets can be fitted to the upstream, downstream or both sides of filters. Sealing mechanisms are not interchangeable and should be recorded at Installation Qualification. This requirement applies to room filters and clean air devices.

Protection grilles should be specified if required. They can be fitted to the upstream, downstream or both sides of filters. They are used to prevent accidental damage during fitting and testing.

The HEPA filter housing dimensions should be specified. This should include the length, width and depth of the filter housing. The dimensions are usually specified in mm and should be recorded at Installation Qualification.

A Manufacturer's code often incorporates the above and it is important to check carefully if ordering from a different manufacturer as they specify the variables in different ways.

Filters should be tested to BS EN 1822 and a copy of the test certificate for each filter should be requested on the purchase order.

APPENDIX 3: Repairs

Repairs to the HEPA filter medium are not permitted; however temporary repairs may be acceptable, at the request of the customer, as emergency short term measures as long as no more than approximately 5% of the filter face area is covered. For filters used in more critical unidirectional airflow applications, the area of repair should never be so great as to affect the uniformity of airflow. A replacement filter should be ordered without delay and fitted and tested on arrival.

APPENDIX 4: Witnessing of filter integrity tests

Personnel involved in witnessing filter tests should check the following:

- The fishtail scanning probe, photometer and aerosol generator should be in good condition and within their respective calibration and certification periods.
- The aerosol should be introduced into the air handling plant sufficiently far upstream of the filters to ensure mixing, more than 15 duct diameters upstream from the filters. If this is not possible there should be an alternative mixing system such as sparge pipes.
- The upstream aerosol concentration should be in the range 20µg/l to 80µg/l. This must be measured with the photometer adjusted to the settings determined during calibration. The photometer may be adjusted AFTER it has been established that the upstream concentration is in the prescribed range to use the measured value as 100% for calculation of % penetration.
- The upstream concentration of aerosol should be checked and recorded at each filter at the start **and finish** of each test.
- The filter and seals should be scanned carefully and slowly, recording any leaks detected.
- Leaks through the filter seals may be resolved by careful adjustment of the clamping bolts by suitably trained staff.

APPENDIX 5: Health and Safety

Dioctyl Phthalate used to be used for the DOP test but is no longer recommended due to its toxicity. In the UK it has been generally been replaced with Ondina X 420 oil manufactured by Shell UK Oil Products Limited. It is a European Pharmacopoeia grade of Medicinal White Oil, colourless and practically odourless, containing almost no sulphur, nitrogen or aromatics.
At the time of producing this document the latest Safety Data sheets can be found online at:

http://www.epc.shell.com/default.asp
or
http://www.meadekingrobinson.co.uk/wp-content/uploads/2014/03/Ondina-X420.pdf
http://www.omf.com.tr/assets/upload/services/msds-en-shell-ondina-x-420.pdf